Overcoming of a "surgical dogma" in acute cholecystitis treated in postponed emergency

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AIM: *To demonstrate the overcoming of a surgical dogma related to acute cholecystitis treatment, in particular to the timing of the operation.*
METHODS: *One hundred cases of observed acute cholecystitis, submitted to an emergency postponed laparoscopic cholecystectomy surgery and histological control of specimens to evaluate rate of surgical complications and rate of reconvertion to open surgery.*
RESULTS: *The complications rate observed and the surgical conversion to open technique was only 1% where in 96% of the cases the histological examination of the specimen confirmed the state of acute inflammation. Therefore there was a substantial success rate of laparoscopic therapy even in emergency situations, in spite of an overcoming of the conventional timing within 72 hours of surgery for acute cases, which has few restrictions from some authors. The reasons allowing in safety that time extension were ascribed to the laparoscopic procedure, apt to overcome the anatomo-pathological barriers through an accurate vision of the operative field, and the use of specialized devices allowing the coagulative dissection of inflamed tissues.*
CONCLUSIONS: *Postponed colecistectomy in acute cholecystitis, in extention of the canonical coded timing of 72 hours, confirmed to be a safe and successful procedure, even in emergency, with only rare exceptions.*

KEY-WORDS: Acute Cholecystitis, Laparoscopic Cholecystectomy, 72 hours.

Introduction

The procedure of surgical treatment for acute cholecystitis, has a surgical timing up to now universally accepted within 72 hours from the onset of symptoms or, alternatively, from the stabilization of patient's conditions and remission of phlogosis through medical therapy, postponing in fact the surgical solution until a quiescence state. Mini-invasive surgery allows to overcome this "surgical dogma" (at least in our experience), operating successfully even after 72 hours with benefits in clinical situation and without inflicting any additional risks to the patient. Considering that, the micromorphological profile of 100 cholecystectomy patients with an acute clinical diagnosis were analyzed by comparing technical and mechanical aspects of conventional surgery with minimally invasive approach, supported by the fundamental contribution of anatomopathological study, and proposing a reformulation of the surgical moment for that pathology.

Devices and Methods

In our case studies, during 180 days were evaluated: 100 operated patients for acute cholecystitis clinically confirmed in 96 cases, 25 as acute and 71 as chronic cholecystitis. The remaining 4 cases were not suggestive either of acute or chronic condition on anatomopathological basis. Ninetyeight cases were in fact lithiasic cholecysti-

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tis and 2 symptomatic alithiasic cholecystitis. All anatomic specimens were submitted to histological evaluation in order to an histopathological typing of the phlogosis degree, together with the typing of microvascular remodelling phenomenon and its correlation with the surgical approach.
We have re-evaluated techniques and devices more frequently used in conventional approach for the detachment of cholecyst from the hepatic bed and isolation of elements from hilum comparing them with laparoscopic devices still used in many surgical fields. Metzenbaum scissors and detachment flock or Finocchietto dissector in open surgery, with an impact surface between 4-6 mm; dissectors or crochets in laparoscopic surgery with an impact surface between 0.7-2 mm.
For each case were examined the onset time of symptoms, ranging in 4.07 days (range 2-14), the average operating time of 91.5 minutes (range 36'-486'), days of hospitalization with an average of 3.4 (range 2-8), the number of drainages used (78 cases, one per patient in subhepatic area), surgical conversions in open technique, complications occurred: only 1 case due to partial lesion of the main biliary pathway.
A discrepancy in interpreting standards used to classify acute situations between the surgical and pathologic interpretation was evident. For the clinical point of view "acute cholecystitis" is defined according to clinical evidence, anamnestic and imaging data, and by intraoperative findings with evidence of tissue edema, often associated with adhesion phenomena with adjacent structures and an increased fragility and hemorrhage in the operating theatre. For pathologic point of view the definition of phlogosis is based firstly on macromorphological features but especially on the detection of cellular elements distinctive of chemiotaxis phenomena, associated with modifications in microvascular reticulum, in some cases with evidence of reparative phenomena related to healing of the phlogosis. An absence of tissue repair mechanisms was typically noticed in recurrent or chronic phlogistic cases. According to the above observations, a possible subdivision into 4 classes of lithiasic cholecystic disease (Tab. I) was identified, that gathers the two interpretations of the same problem and which requires some explanations: in our observations we considered only cholecystectomies performed on patients with preoperative diagnosis of "acute" cholecystitis; in the 2nd class we enrolled all cases with a clinical acute diagnosis leading patients to the operating table after a single typical episode of biliary colic; in the 3rd class we included cases of recurrent symptomatic biliary pain and in the 4th class clinical cases with a last "acute" episode during hospitalization.
An careful observation of surgical specimens gave the opportunity to distinguish findings in two main groups, the first referred to "acute" phlogosis and the second to chronic phenomena, and among these two groups it was possible a further distinction in several subgroups according to histological peculiarities of each type.

Tabella I

Class	Pathology Type	Surgery Classification	Anatomopathological Classification
I	Cholecyst Calculosis		
II	Primitive Acute Cholecystitis	26	10 Exudative 9 Gangrenous
III	Chronic Cholecystitis	44	54
IV	Recurrent Acute Cholecystitis	30	26

Acute Cholecystitis

Acute Calculosis Cholecystitis (90-95%): the major clinical complication in cholecyst calculosis and the leading cause of emergency cholecystectomy. It mainly interests women between sixty and seventy.
Acute Acalculous Cholecystitis (5%): it is subsequent to various pathological situations such as major trauma, debilitating conditions, burns, diabetes mellitus, systemic infections and use of cocaine.

The anatomopathological alterations of the two above forms are similar. At histologic examination the cholecyst is often relaxed and edematous. Serosa presents a hemorrhagic appearance and it is covered by serous exudate. Subserous blood vessels are congested and bowel wall is thickened (up to roughly 2 cm) with edema and hemorrhagic extravasations. Mucosa is extensively ulcerated and lumen may be occupied by blood, fibrin, bile and dense material consisting of cholesterol and calcium carbonate. The extent of tiny abnormalities depends on the length and severity of disease. Acute granulocytic inflammatory infiltrate is present only in complicated forms of bacterial infections, while edema and hemorrhagic extravasations are always evident.
Fibrin thrombi are often observed in small-caliber intramural and subserosal veins and a widespread fibroblast proliferation may be a sign of "chronic condition" (fibroblast proliferation appears on the 5th day after the beginning of pathological process and reaches the highest expression on the 10th day). During this stage, several inflammatory factors appear such as lymphocytes, plasma cells, eosinophil and macrophage granulocytes. These pathological abnormalities may appear in a previous chronic form and this occurrence may cause an interpretative discrepancy between clinician and pathologist to define a cholecystitis as acute or chronic.
If not treated, acute forms may lead to complication, such as perforation followed by a biliary peritonitis.

Acute cholecystitis in its thriving stage may result in a focal or diffuse transmural ischemia evolving into a *Gangrenous Cholecystitis.* A superimposed gas-producing bacterial infection, causes acute emphysematous cholecystitis.
There are forms where bacterial infection causes the formation of abundant exudate that fills the gallbladder lumen reflecting an entity known as *Cholecystitis Empyema.*

Chronic Cholecystitis

It is the most common disease of cholecystitis, primarily correlated to calculosis, and may be a less frequent sequela of recurrent episodes of acute forms.

The macroscopic aspect of cholecystitis depends on the severity and duration of inflammatory disease. Gallbladders may appear almost normal or with fibrous thickening, and in severe cases present distortion of the wall, considerably thickened, with scarred alterations of serosa as a result of adhesion phenomena on the surrounding anatomical structures. Mucosa presents a granular or ulcerated surface with "pseudo-polyploid regenerative" areas. In a small percentage of cases diffuse dystrophic calcifications in the lamina propria and muscular tunic are observed, a condition defined "*Porcelain Cholecyst*" associated with a higher risk of developing glandular cancer.
The histological aspect includes various degree of intensity of chronic phlogosis represented mainly by T lymphocytes with plasma cells, histiocytes and some eosinophils. Sometimes phlogosis is so weak that the distinction between a chronic cholecystitis of minor entity and a normal cholecystitis is observed dependent.
The presence of neutrophil granulocytes refers to a chronic form in which an obstruction of the lumen caused by calculosis should be suspected. In some cases the appearance of numerous macrophages containing bile and lipofuscin are observed in the so-called *"Cholegranulomatous Cholecystitis".*
The degree of fibrosis is variable and in long-lasting chronic forms may be observed the obliteration of small vessels lumen and neural hyperplasia phenomena.
The epithelium of the cholecyst may be normal, atrophic, metaplastic, with focal ulceration or regenerative aspects.
"Diverticular" aspects of the epithelium defined as "Rokitansky-Aschoff Sinuses" are usually present and more prominent in severe chronic forms. Marked diverticular aspects associated with hypertrophy or hyperplasia of muscular tunic are defined as *"Adenomyomatosis*".

There are "variants" of chronic cholecystitis:
– *Follicular Cholecystitis*: in chronic forms the lymphocytic infiltrate is steady, but in rare cases (0.1-1.0%) several lymphoid follicles appear in the lamina propria of the bowel wall producing a "pseudolymphomatosis" aspect. Associated in the past with typhoid fevers, it is now present in some infections caused by Gram-negative bacteria and in sclerosing cholangitis.
– *Eosinophilic Cholecystitis:* eosinophil granulocytes are present in the inflammatory infiltrate of common cholecystitis, while a predominant eosinophilic component is rather infrequent and evident in a small percentage of cholecystectomies (5-10%). Some of these forms are associated with peripheral hypereosinophilic syndromes including various allergic conditions and true hypereosinophilic syndrome. Parasitosis and hypersensitivity to some drugs are sometimes present. There are however forms of hypereosinophilia not related to previous conditions, found both in calculous and acalculous forms of cholecystitis.

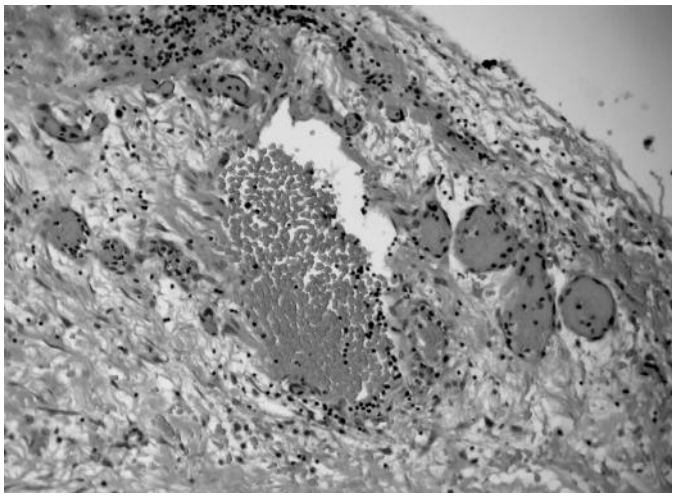

Fig. 1: The growth of small capillary vessels in subserous area (Ematossilina Eosina 40X).

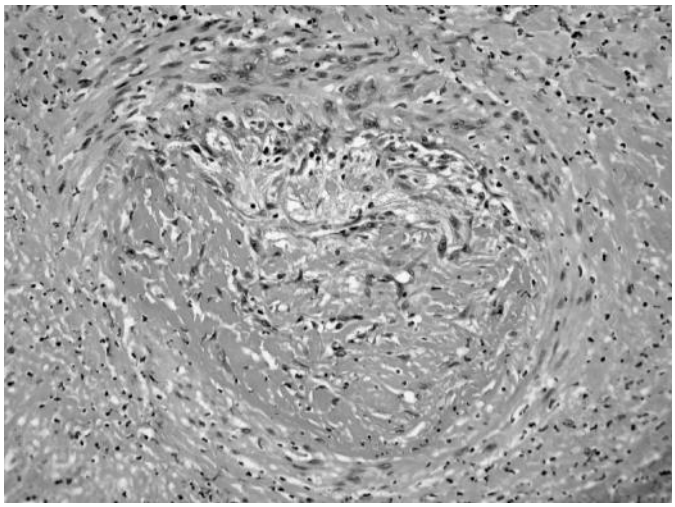

Fig. 2: Vascular intramural thrombosis in a medium-caliber vein. (Ematossilina Eosina 40X).

The eosinophilic infiltrate may only interest mucosa or muscular tunic, but in some cases it is transmural, associated with a myofibroblasts proliferation.
– *Xanthogranulomatous Cholecystitis:* it is a form characterized by the presence of numerous "foamy histiocytes" often associated with calculosis. The mucosal ulceration or rupture of Rokitansky-Aschoff Sinuses with subsequent bile extravasations in the layers of the wall may be factors stimulating the accumulation of histiocytes whose lumen contains cholesterol, bile salts, iron and choroid pigments. Among the histiocytes other inflammatory factors are present and may be observed a fibroblast proliferation during the chronic stage of illness.
– *Cholecystitis in Infectious Processes*: many cholecyst infections are secondary to other pathological processes such as calculosis or bowel neoplasia with superimposed infection or infections in other districts of the digestive tract such as salmonellosis or some parasitosis (giardiasis, schistosomiasis and amebiasis), and some viral forms (EBV, hepatitis A and cytomegalovirus).
– *Cholecystitis in Idiopathic Inflammatory Diseases*: chronic aspecific phlogosis may interest cholecyst in inflammatory idiopathic diseases affecting the digestive apparatus such as the Chron's disease, ulcerative rectocolitis, sclerosing cholangitis and primary biliary cirrhosis.
– *Vasculitis in Phlogosis Process of Cholecyst*: vasculitis can be observed during a cholelithiasis, but also as acalculous cholecystitis. Phlogosis affecting the vascular wall of intramural arterial vessels is more frequently a local phlogosis phenomenon rather than a systemic form expression, as can be observed in so-called collagen disease (rheumatoid arthritis, systemic lupus erythematosus, Henoch-Schonlein purpura and Wegener's granulomatosis).
– *Ischemia and Infarction*: although the presence of necrotic areas is often related to the degree of phlogosis process, an ischemia of cholecyst wall and, as a secondary event, an arterial thrombophilia in intramural arterioles probably favored by the local release of chemicals that can encourage the development of endovascular thrombus may be rarely observed. Histologically this occurs mainly in combination with an acute erosive-ulcerative phlogosis of the wall with presence of acute and chronic intense inflammatory infiltrate. Other causes of wall infarction can be associated with ischemia caused by a bladder torsion (volvulus), surgical operation or abuse of cocaine. In relation to the etiopathogenetic cause and its intensity, cholecyst infarction can be localized or diffuse. The more significant wall alterations include necrosis mainly interesting the epithelium and lamina propria substituted by granulation tissues.

Discussion

Our experience demonstrates positively the possibility to overcome the time window of 72 hours, up to now considered impossible to exceed, from symptoms onset until the cholecystectomy surgery for acute cholecystitis. In the cases treated, 28 were led to operating table on the 7-8th day after the appearance of clinical with an overall rate of complication, conversion or "second-look surgery" equal to 1, which is however not properly referable to this "over time treatment" group. It is well known, even on the basis of information gathered from literature, that the early surgical intervention in traditional surgery could benefit from the tissue edema according to an interpretation of the surgical technique procedure of detaching the viscus, with main haemostatic time devolved to the identification of arteriolar trunk of cystic artery and potential supernumerary vessels. The advent of the mini-invasive technique has modified that logic by replacing detachment with dissection, associated with hemostasis of capillaries through electro-fulguration and/or clipping of larger branches. The tissue detachment-coagulation, in a first moment was performed preferentially using a hooked device, and then with a certain propensity to the "distraction" of coagulated tissues, while technical development has gradually led to the adoption of the dissection manoeuvre, which uses a thin prehensile device with 2 branches allowing both an efficient bevel progression manoeuvre, as well as a useful electro-fulguration. There are two steps which present some difficulty of manoeuvre: the first concerns the visibility of adhesion sites, and the second the clear identification of Calot's triangle elements and the control of hemostasis in surgical focus. This last condition results more difficult because of modification in vascular reticulum, as described in vascular anatomopathological observations of our case study and literature. These difficulties are referable both to an increase in overall vascular volume, due to a local microcirculatory venous congestion as a result of hyperflux towards inflamed tissue and frequent microthrombus phenomena, and to the abundant representation of hemorrhagic extravasations often sustained by real inflammatory vasculitis and perivascular processes. The technical innovation introduced with the videolaparoscopy is the opportunity to reduce the device impact surface on the inflamed tissue as much as 50-80%; this theory is supported by the well known mathematical rule of inverse proportionality that, given 3 variables:
A) Tissue of cholecyst
B) Impact surface (surgical devices)
C) Vascular reticulum

$$B = aA/C$$

This mathematical deduction is based on the postulate that at the same cholecyst size, if the volume of the vascular reticulum doubles, the impact surface has to be reduced to maintain an effective result.
The approach to the vascular compartment is then modified, which is the major cause of difficulty and danger

during acute cholecystectomy implemented after 72 hours from the onset of symptoms. The standard laparoscopic approach, as it was carried out in our case study, faces and neutralizes with a centripetal progression against the hilum, the newly formed thin vascular reticulum, typical of phlogosis conditions. In literature, the question of timing seems to be rather controversial with some surgical opinions still more favorable to a prudent attitude towards 72 hours, considering 48 hours as a final operability limit. According to our point of view, in some rare cases data have been published about the extension of this time up to 5 days using videolaparoscopic technique, with a conversion rate around 12% and surgical time on average higher than 15'-75'. Cheema S., even though recognizes the correctness of the methodology in emergency cholecystitis, believes that biliary lesions are still independent from the surgical timing but not the probability of conversion to open surgery, reporting of 3 biliary complications on a case study of 120 emergency cholecystectomies performed for acute cholecystitis with a conversion rate of 27%. As argued by Orlando R., the thesis supporting surgical timing for this pathology was authoritatively based on "Vascular Issue", condition well marked during the anatomopathological observations of our case study, in which phenomena of vascular architecture remodeling, typical of phlogosis, contribute to obstacle the identification of the surgical anatomy of the operative field, especially after the 72nd hour from onset of illness, discouraging when possible surgical solution.
Here, a concluding consideration on the discrepancy in the diagnosis of acuteness, particularly on the first observation of disease, where the clinical doubles acute diagnosis than the pathological anatomy: we believe this may be due to a diagnostic error deriving from an incorrect interpretation of a proximal digestive tract pathology or an erroneous interpretation of a colic-hyperkinetic pain of cholecyst after abnormal digestive stimulus, or as described in literature as a consequence of a lithiasic movement towards the infundibulum after a valve movement with a painful evocation to a transient distension of cholecyst. It is still to be considered the pain caused by microlithiasic transit from Vater's papilla with a transitory hypertensive endocholedochal condition; these are all events, however, generally attributable to the category of erroneous clinical interpretation. The clinical picture is probably overestimated because of an improper evaluation of echographic data associated with a painful connotation, even without an evidence of wall phlogosis. Our case study seems on the contrary to agree with the diagnosis of acute relapse evidently due to a chololithiasic pathology which results have to be ascertained.

Conclusions

The overcome of the apparently conventionally highly advisable limit of 72 hours, in order to safely intervene in acute cholecystectomy cases, has been successfully demonstrated in our case study of 100 acute cholecystectomies routinely performed using videolaparoscopic technique. In one case we had to resort to surgical conversion after an accidental partial lesion of the main biliary tract. The average surgical times were of 91.54', the average postoperative period of bed rest was of 4.7 days with a complication rate of 1% due to an incomplete primary biliary lesion. The reason of our operative choice beyond the time limit conventionally agreed is based on the relevance of coagulation time that becomes the key manoeuvre than the open technique, combined with the dissection devices that present a significantly reduced impact surface. The evaluation of clinical diagnosis in front of the pathological one has pointed out a discrepancy in particular on the definition of "acute cholecystitis", with a marked relevance of the microscope findings in the report, in our opinion due to a combination of factors often related to subjective interpretation of clinicians.
We have referred to the mathematical rule of inverse proportionality to demonstrate the merits of both time and technical choice. A subdivision into 4 classes of acute phlogosis phenomena of cholecyst has been proposed, within which a multitude number of pathological variables were described, observed and described in literature.

Riassunto

Lo scopo di questo lavoro è la dimostrazione del superamento di una "norma chirurgica" riferita al trattamento della colecistite acuta. A tale scopo abbiamo preso in considerazione 100 casi di colecistiti acute, presentatesi alla nostra osservazione, e sottoposti a intervento di laparocolecistectomia in urgenza differita con successiva indagine istologica. Da questo approccio, sono scaturite alcune considerazioni riferite alla classificazione combinata anatomo-chirurgica, al sostanziale successo della terapia laparoscopica anche in regime di urgenza ed in particolare si è dimostrato il superamento della necessità della osservanza del tempo canonico di intervento per questa patologia, sino ad ora codificato entro le 72 ore, con alcune rare restrizioni di alcuni autori. Abbiamo valutato quelli che, a nostro avviso, sono stati i motivi che hanno consentito la dilatazione di tale tempo in regime di sicurezza, da ascrivere sia alla metodica che ben si presenta al superamento degli ostacoli anatomici nel corso di questa forma morbosa, grazie all'accurata risoluzione visiva e alla fine, strumentazione dedicata, che ben si presta alla dissezione coagulativa del campo chirurgico, in accordo con le evidenze neoangiogenetiche dell'istologia.

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